Plaque Stabilization and Preemptive BVS: From Stable to PREVENT

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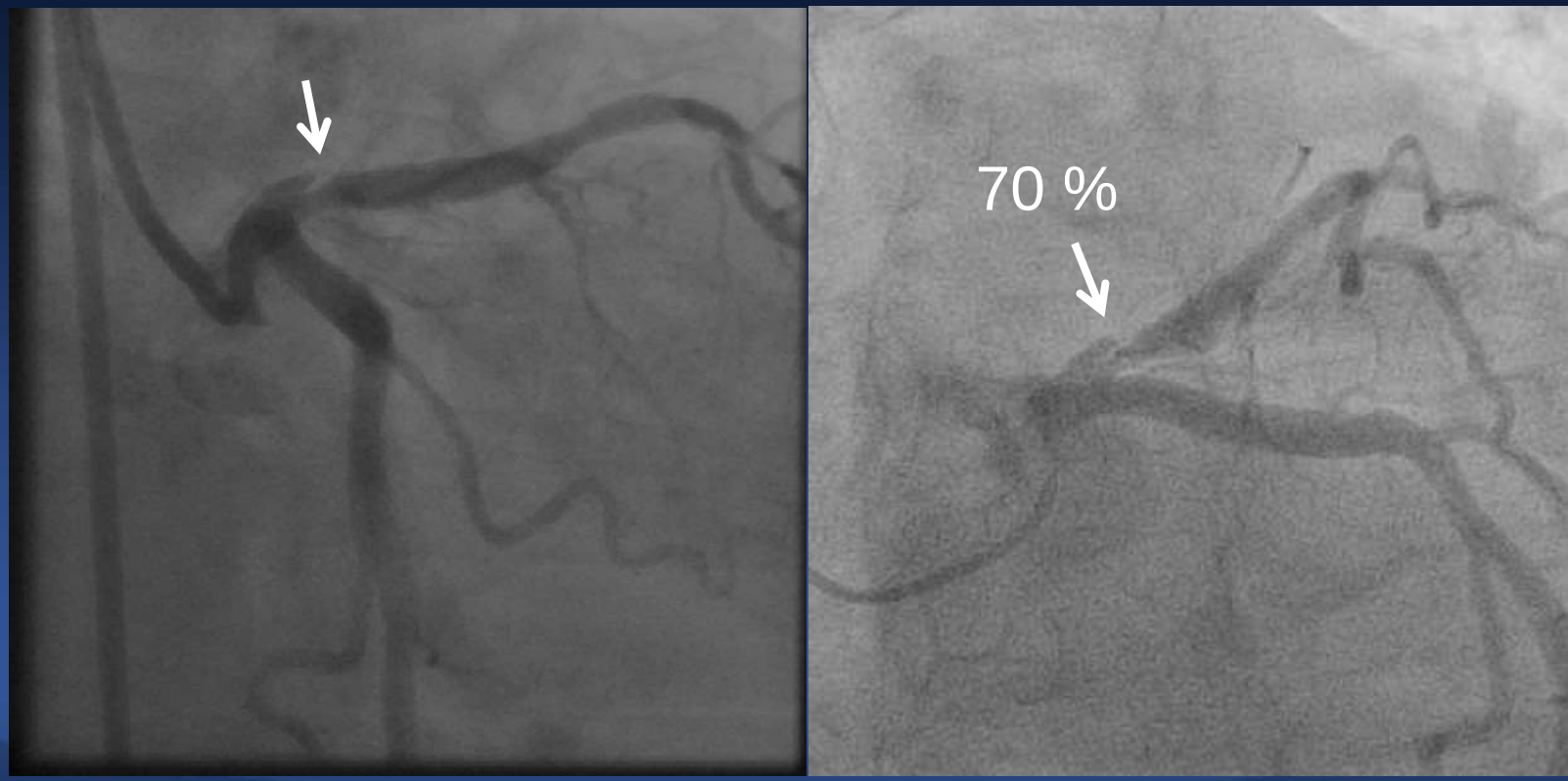
M/74,
Asymptomatic Plaque Rupture

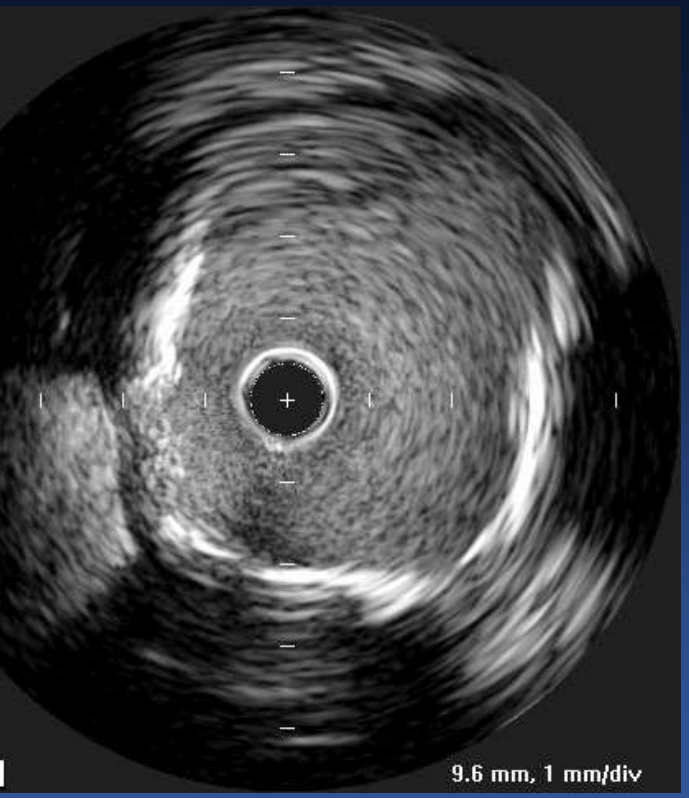
Proximal LAD Stenosis on Coronary CT,
Hypertension, DM, Hyperlipidemia, Ex-smoker

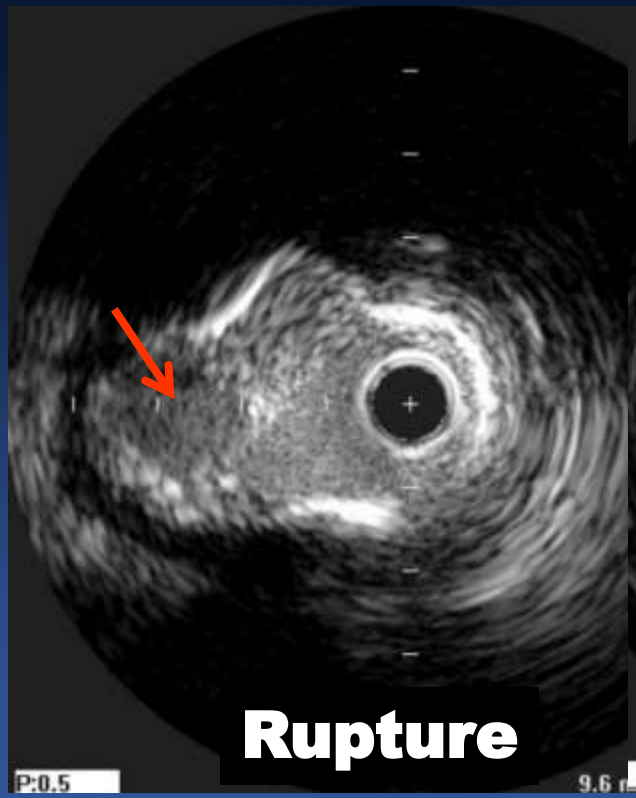


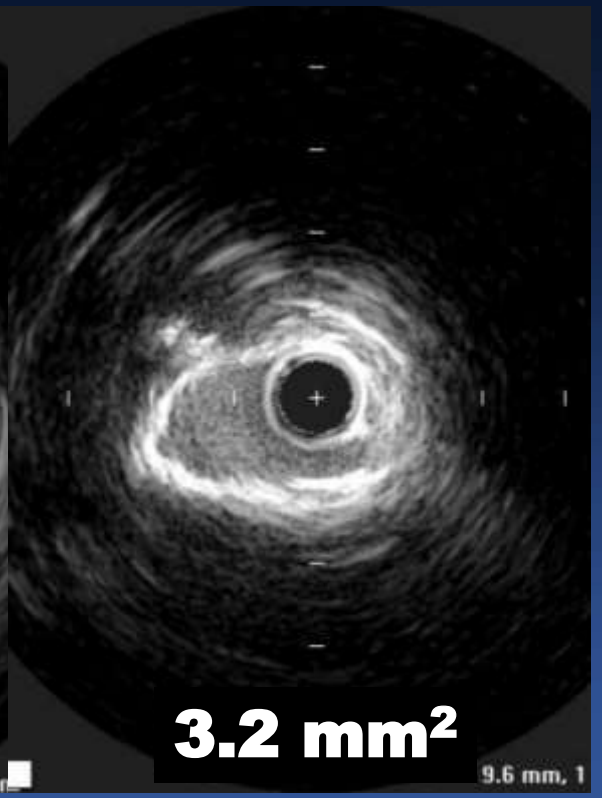
IVUS

LM

LAD, Culprit





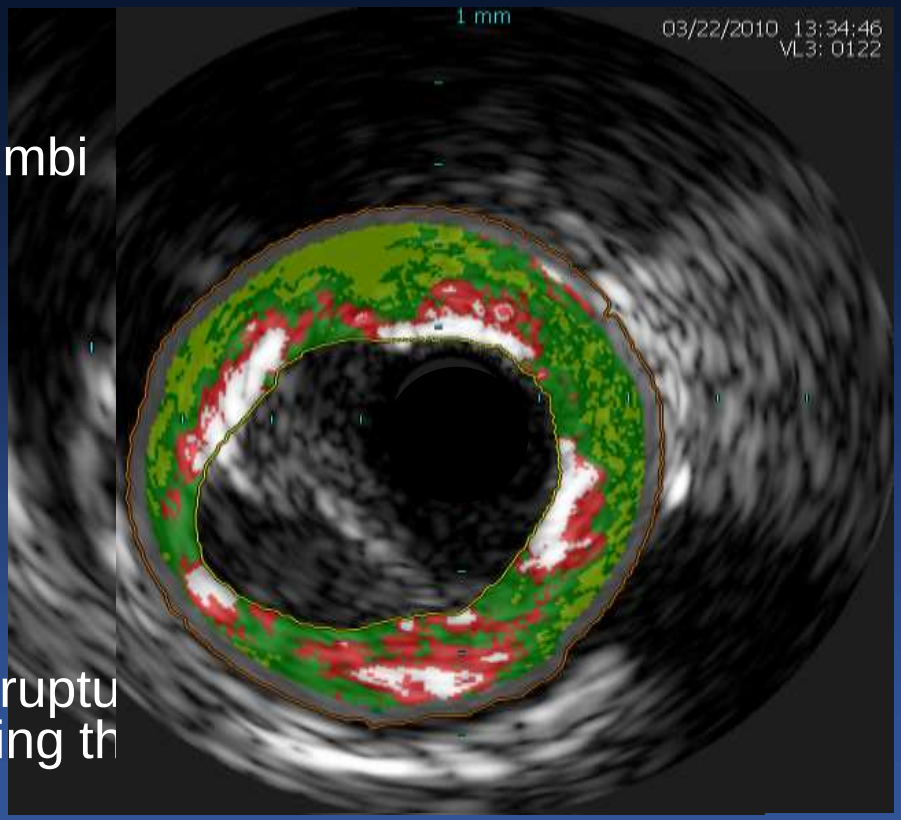


VH-IVUS

LAD, Culprit

Thrombi

Plaque ruptu
organizing th



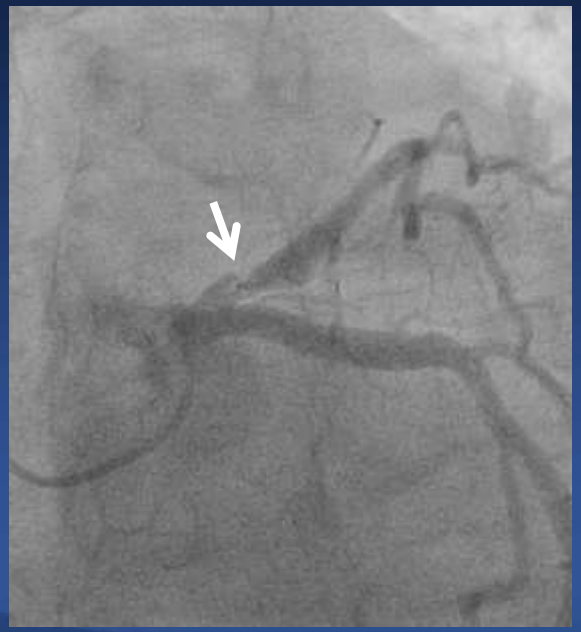
PB: 71.3%
FI : 41.4%
FF: 20.0%
NC: 23.0%
DC: 15.6%

Vulnerable Plaque !

Functionally Insignificant Vulnerable Plaque

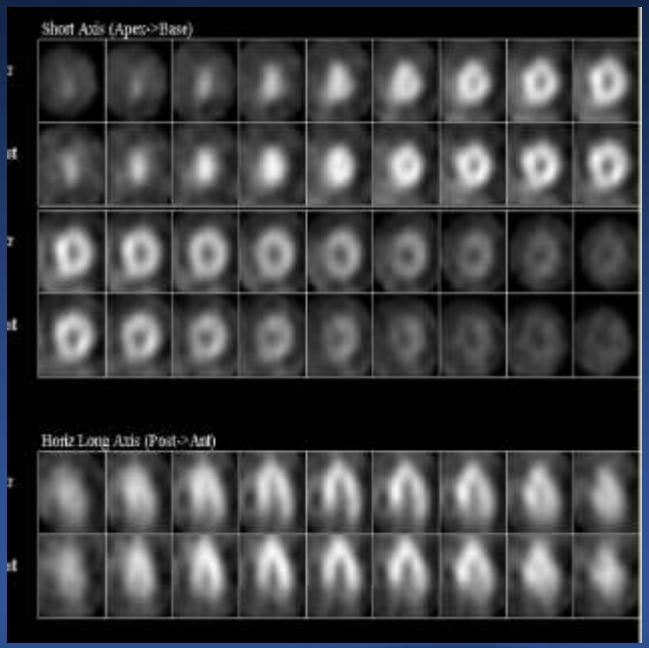
To Treat or Not To Treat Just Defer!

Vulnerable Plaque



Negative FFR 0.89

Normal Thallium Spect

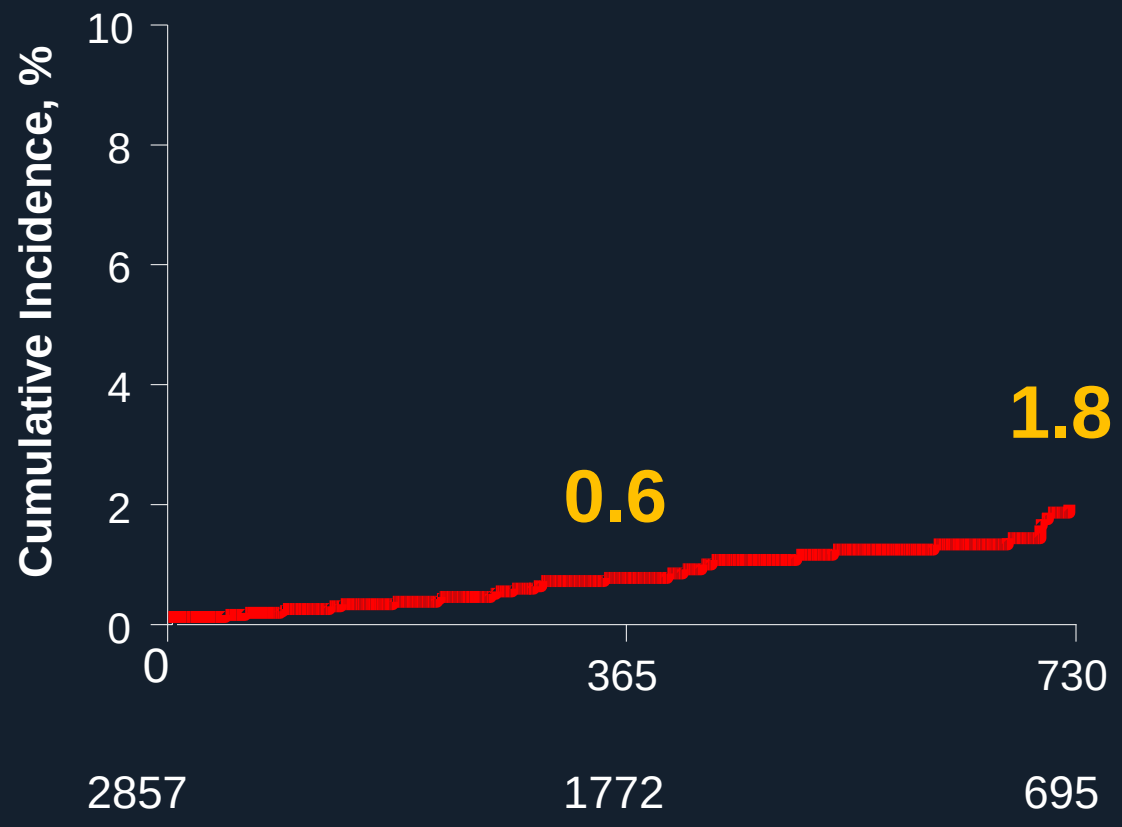


Why I Defer ?

1. I am a FFR believer.
   Defer is Safe and Good ! We have Data.
2. FFR is *well matched with non-invasive stress tests.*
3. Negative non-invasive stress tests means *just excellent prognosis (0.6%/year, Cardiac Death and MI),* even in the presence of angiographically proven coronary artery disease.

Shaw LJ, J Nucl Cardiol 2004;11:171-85 ,
Prognostic value of gated myocardial perfusion SPECT.
Very large meta-analysis. (n=39,173 patients)

Cardiac Death and MI at 2 Years
(2857 patients, 3534 DFERred lesions)



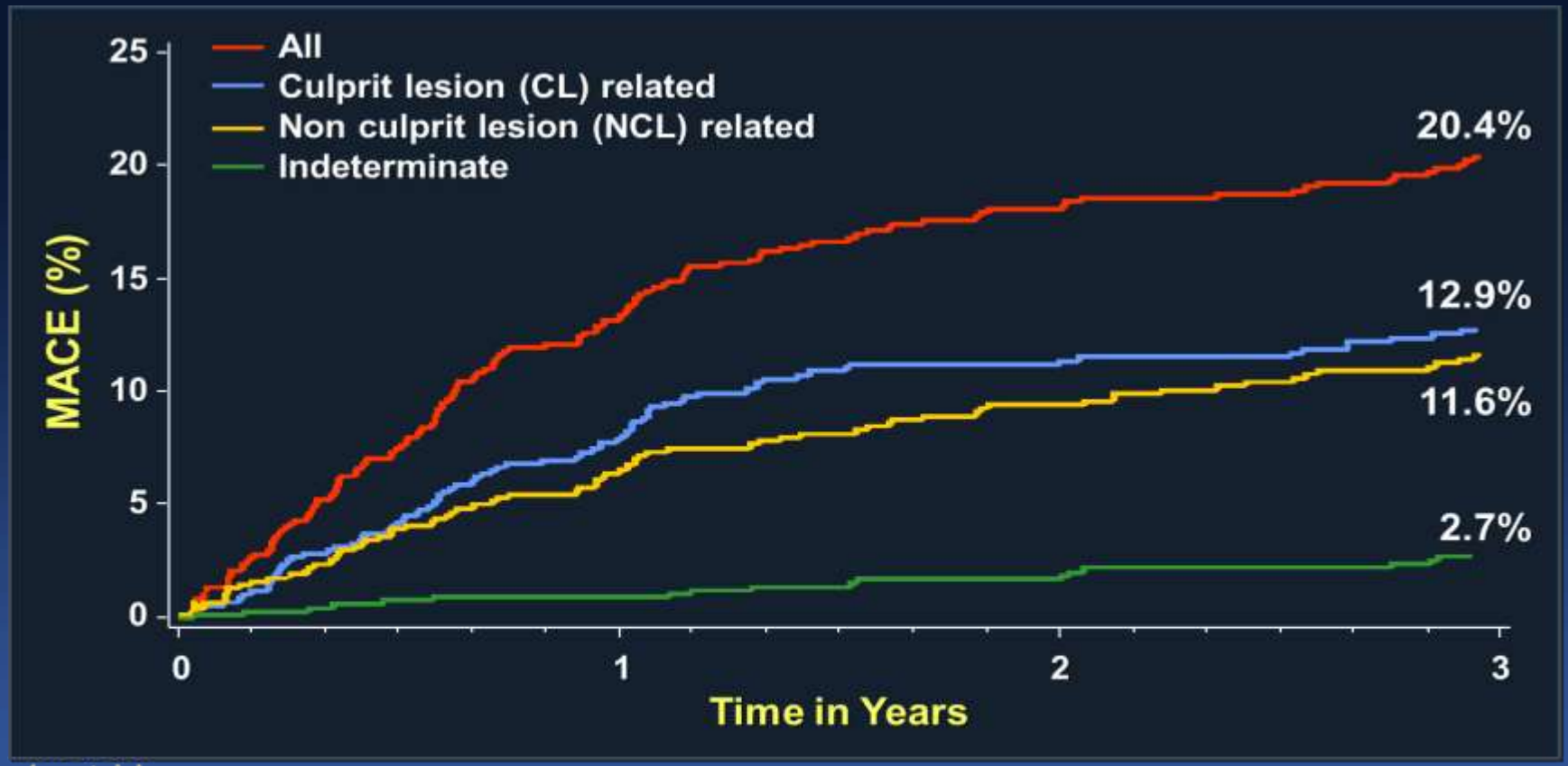
Death and MI /yr

Negative FFR (>0.80 or 0.75) or Negative Non-Invasive Stress Tests: (NUCLEAR studies, DEFER, FAME)	**< 1 %**
Stented Segment : (DEFER, FAME, SYNTAX, and registries)	**2-3 %**
Untreated Positive FFR (<0.75 or 0.80) or Positive Non-invasive Stress Tests: (Registries, ACIP, etc)	**5-10 %**

Should We Treat *Functionally Insignificant Vulnerable Plaque* ?

PROSPECT: MACE

(N=700, ACS, 3-Vessel Imaging after PCI)

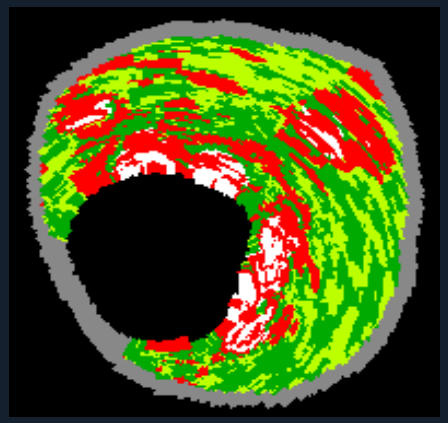


Number at risk				
ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

Stone GW et al. NEJM 2011;364:226-35

Vulnerable Plaque
Defined by VH-IVUS

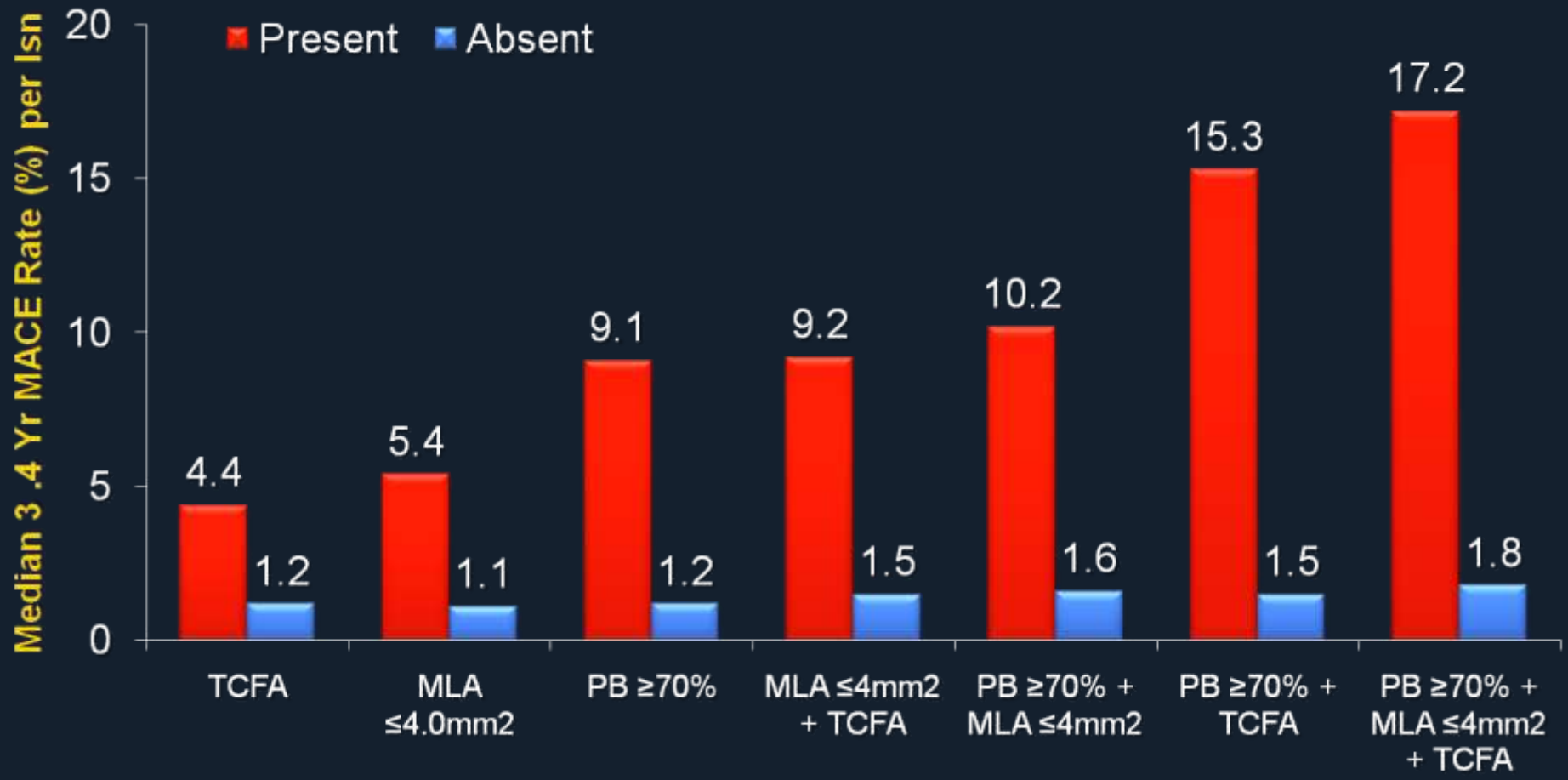
Independent Predictors of Non-Culprit Lesion Events



	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Stone GW et al. NEJM 2011;364:226-35

PROSPECT: Correlates of Non Culprit Lesion Related Events



	TCFA	MLA ≤4.0mm2	PB ≥70%	MLA ≤4mm2 + TCFA	PB ≥70% + MLA ≤4mm2	PB ≥70% + TCFA	PB ≥70% + MLA ≤4mm2 + TCFA
Prevalence*	51.2%	49.1%	30.7%	17.4%	15.4%	11.0%	4.6%
Lesion HR	3.8 (2.2, 6.6)	5.0 (2.9, 8.7)	7.9 (4.6, 13.8)	6.4 (3.4, 12.2)	6.7 (3.4, 13.0)	10.8 (5.5, 21.0)	10.8 (4.3, 27.2)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA

PROSPECT II Study

PROSPECT ABSORB

900 pts with ACS after successful PCI

3 vessel IVUS + NIRS (blinded)

≥1 IVUS lesion with ≥70% plaque burden present?

Yes (N=300)

R 1:1

- ABSORB BVS + GDMT (N~150)
- GDMT (N=150)

No (n=600)

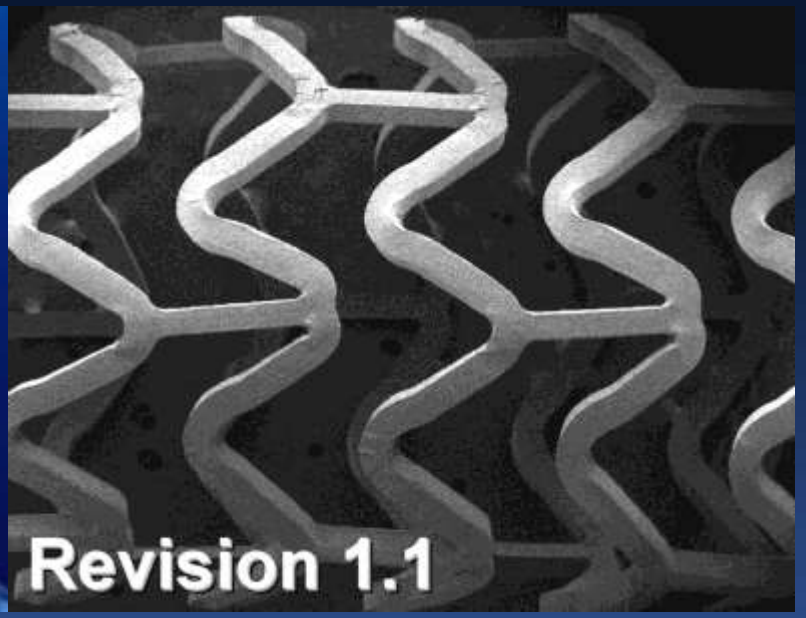
Routine angio/3V IVUS-NIRS FU at 2 years

Clinical FU for up to 15 years

Hypothesis,

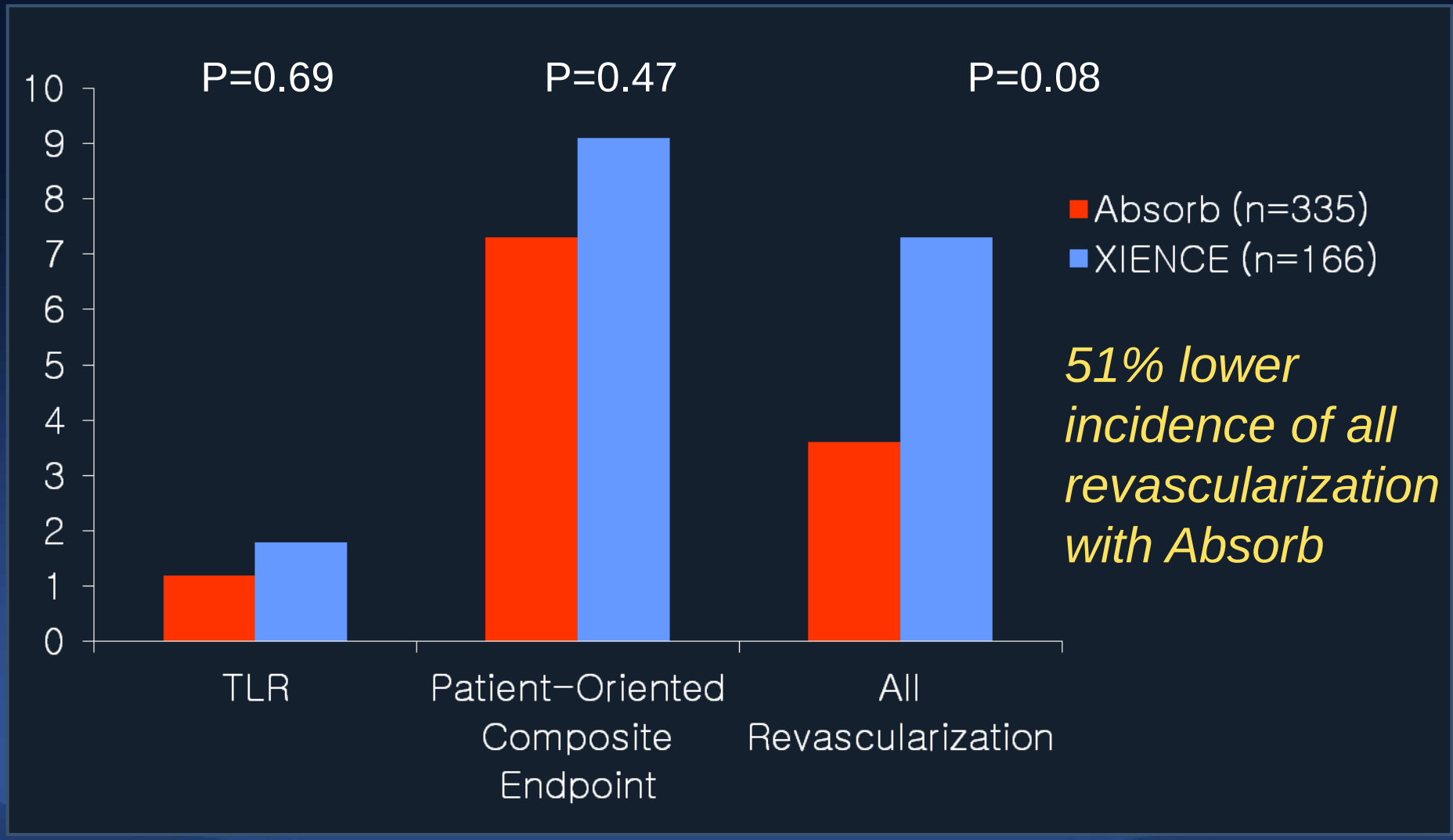
BVS Implantation Can Stabilize Plaque Vulnerability Which May Prevent Future Events of Vulnerable Plaque.

Abbott Absorb, Everolimus Eluting BVS



PLLA ; Poly (L-lactide), Multi-link pattern, 150 um

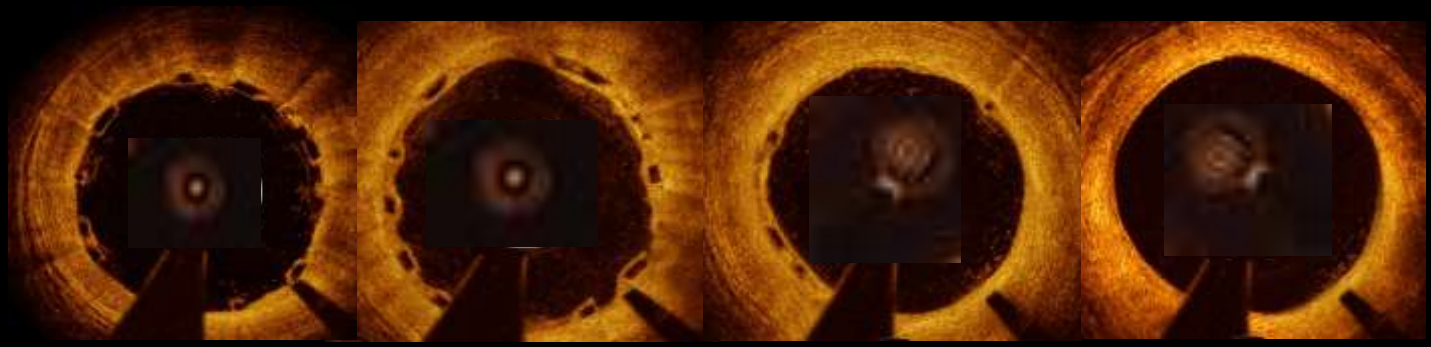
ABSORB II, 1-year Results



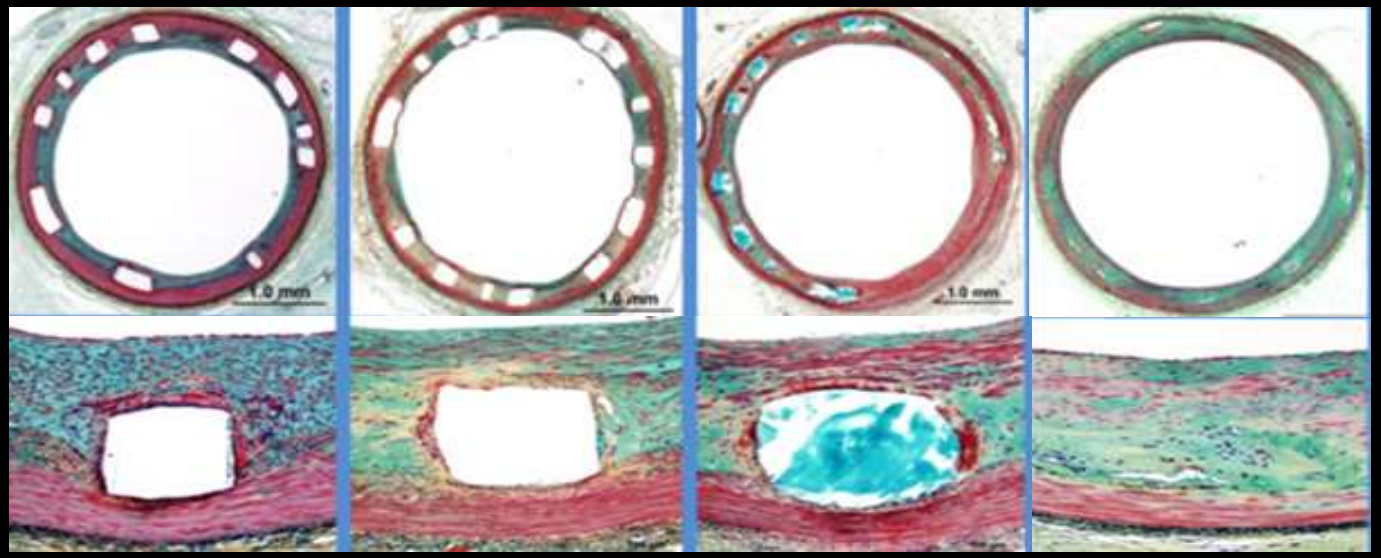
Patrick W Serruys, et al, Lancet Sep 14, 2014

Do their Job and Disappear !

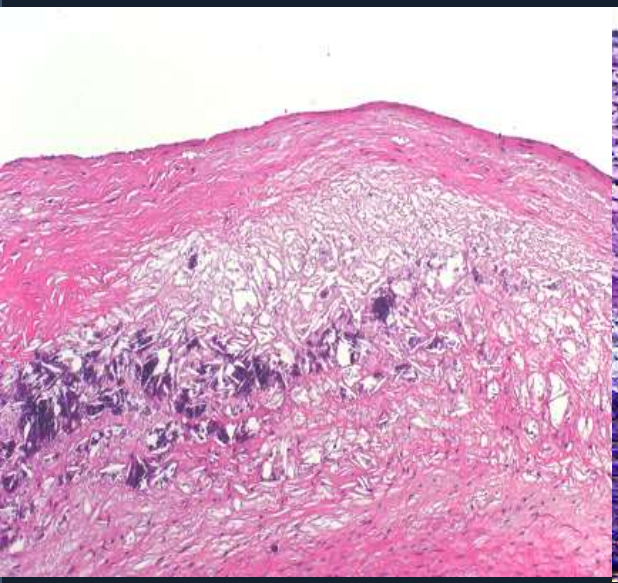
Replaced With SMCs and Myofibroblasts



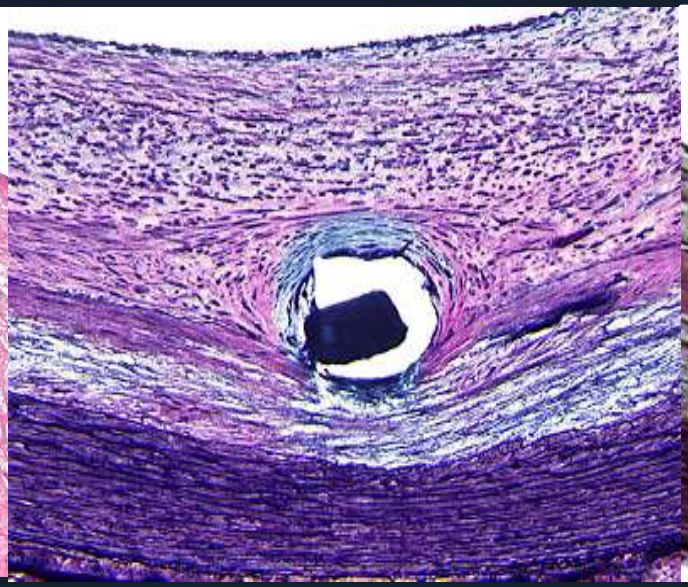
1 month 6 month 2 year 5 year



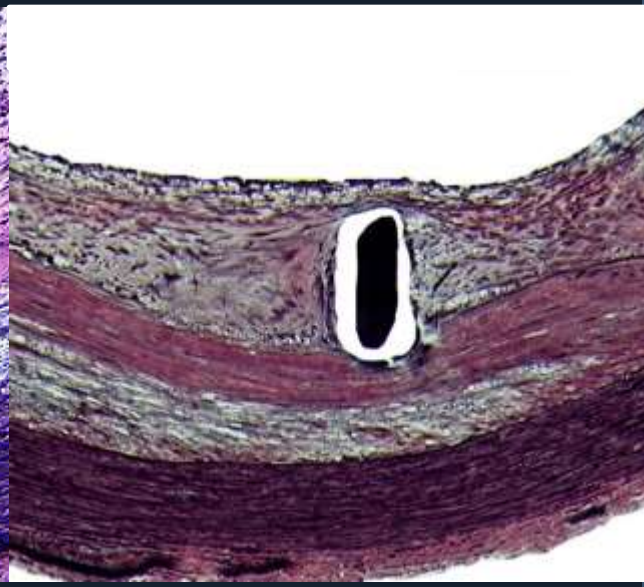
Everolimus Induced Less Neointimal Hyperplasia on TCFA



TCFA



Metallic &
Polymer Strut

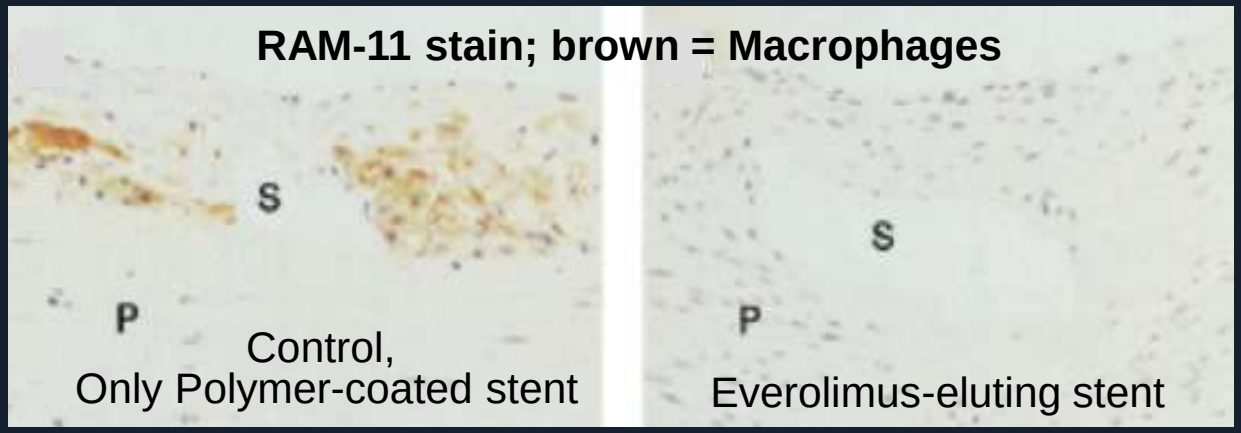


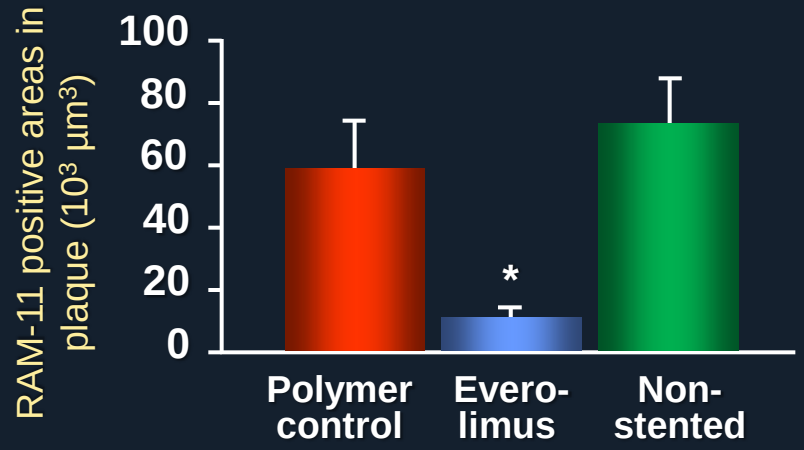
Everolimus Strut

Adapted from Moreno PR.Cardiol Clin 2010;28:1-30

Everolimus Induced, Marked Reduction of Macrophage

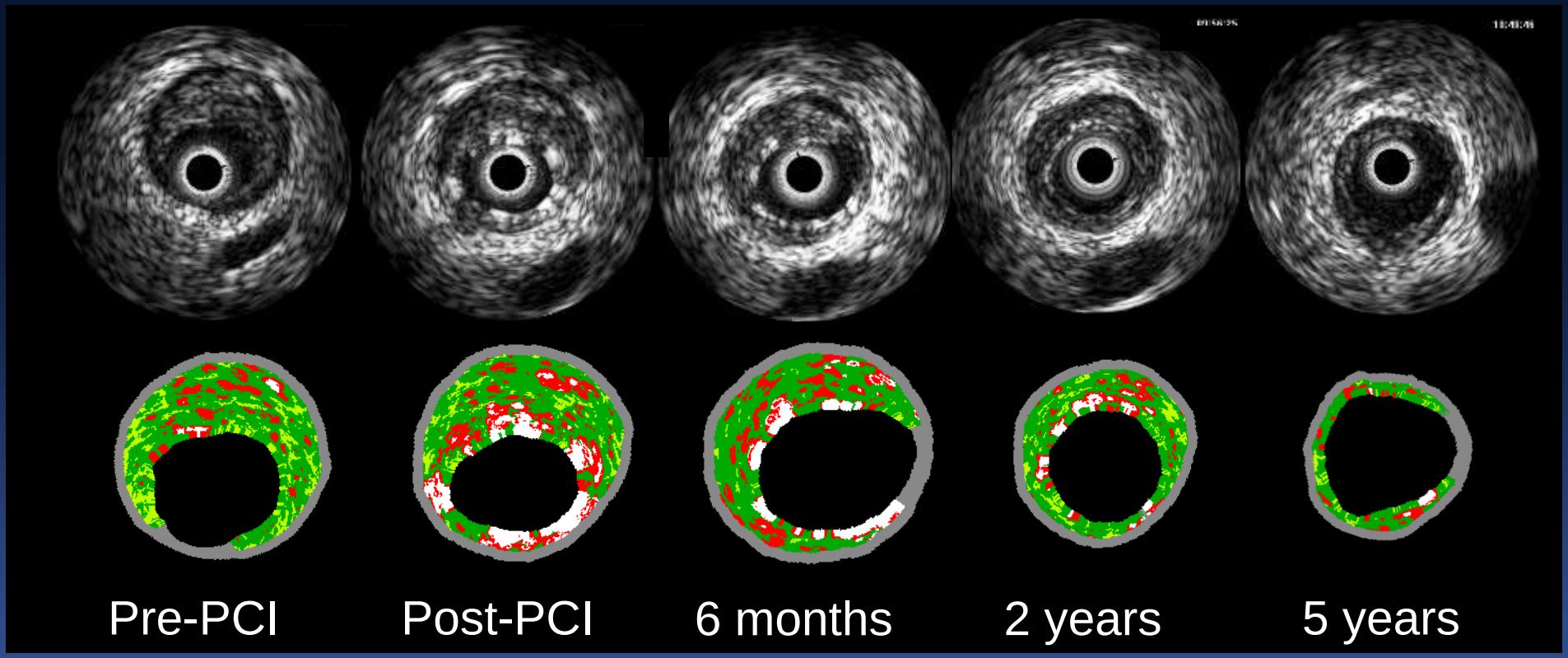
Atherosclerotic arteries of cholesterol-fed rabbits





EES resulted in marked reduction of macrophage content, with preservation of SMC, *which can stabilize the plaque vulnerability*

BVS on Vulnerable Plaque, Plaque Stabilization and Lumen Enlargement



Vessel area (mm^2)	15.72	15.34 (3%)	14.09 (10%)	13.76 (12%) ↓
Mean lumen area (mm^2)	6.95	6.17 (11%)	6.56 (5.6%)	8.09 (16%) ↑
Plaque area (mm^2)	8.78	9.17 (4%)	7.54 (14%)	7.07 (19%)

We Have Data,

Statin Treatment Can Stabilize Plaque Vulnerability.

STABLE Trial

(*ST*atin and *A*theroma Vulnera*B*i*L*ity *E*valuation)
Double-blinded, Prospective, Randomized, Controlled Trial

Total 290 patients with
at least 1 deferred native coronary artery lesion

2:1 randomization (double-blinded)

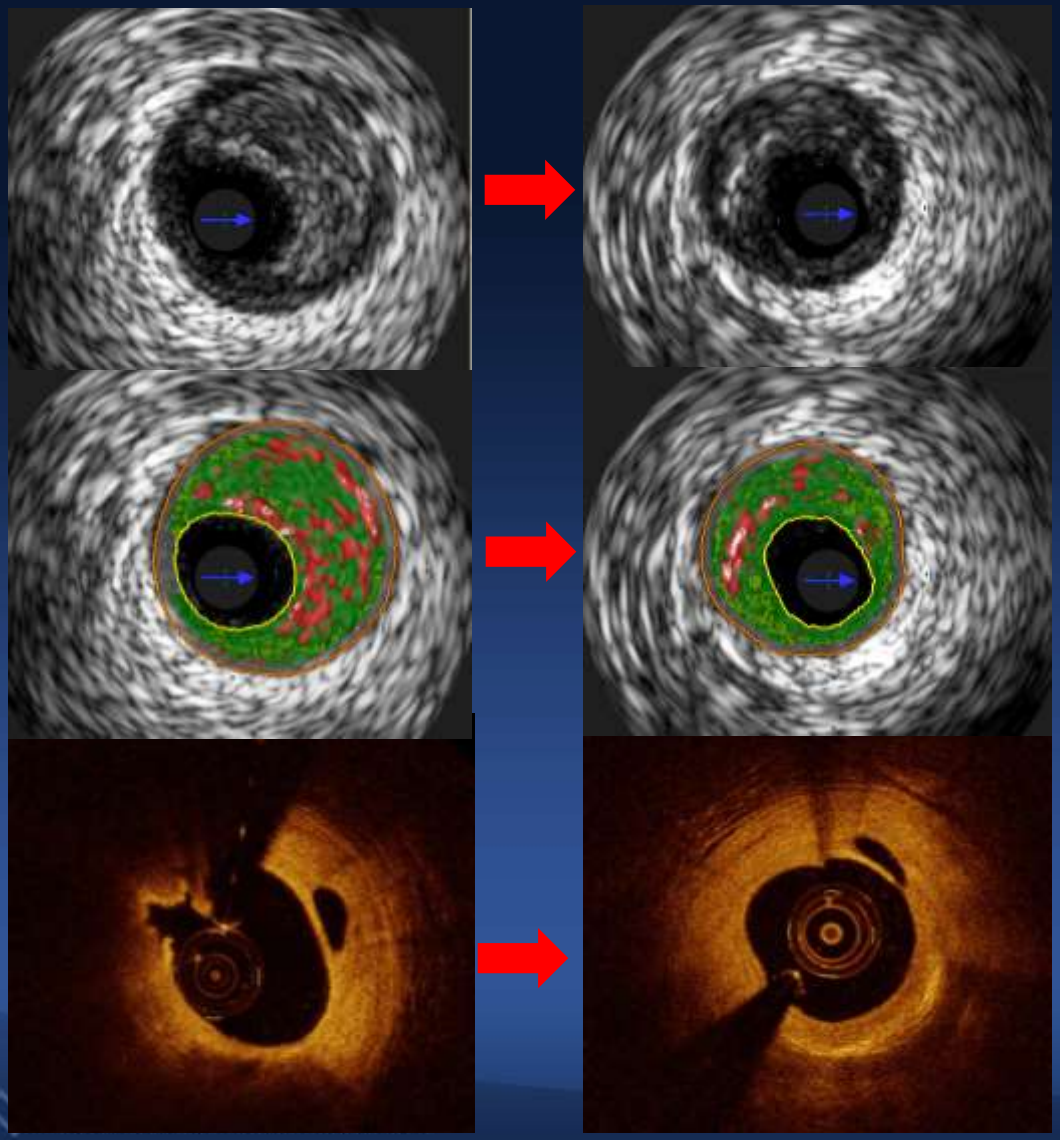
Rosuvastatin 40mg

Rosuvastatin 10mg

VH-IVUS, Conventional IVUS, and OCT
At baseline and 12-month follow-up

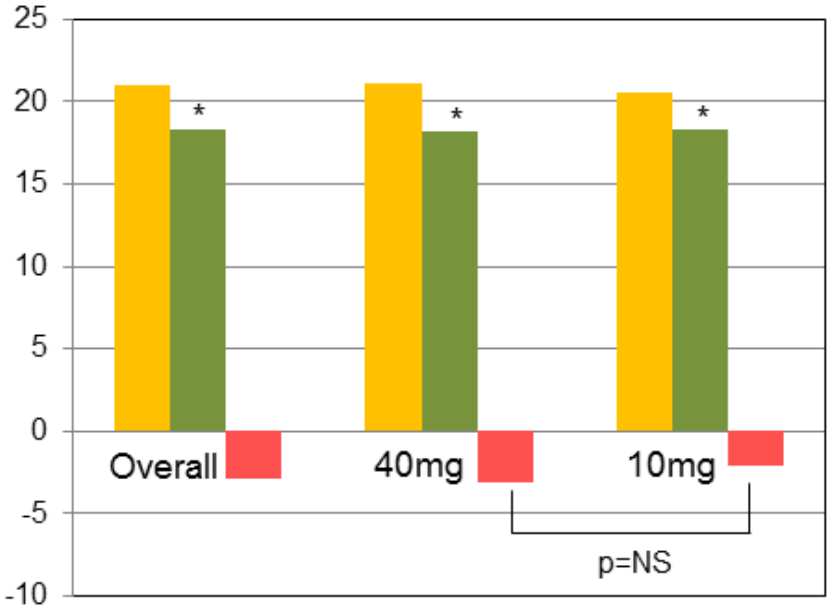
- Primary efficacy endpoint: change in %NC volume within target segment
- Secondary endpoint: change in %NC volume comparing rosuvastatin 40mg vs. 10mg groups

Rosuvastatin Therapy Can Make A Plaque Regression and Stabilization

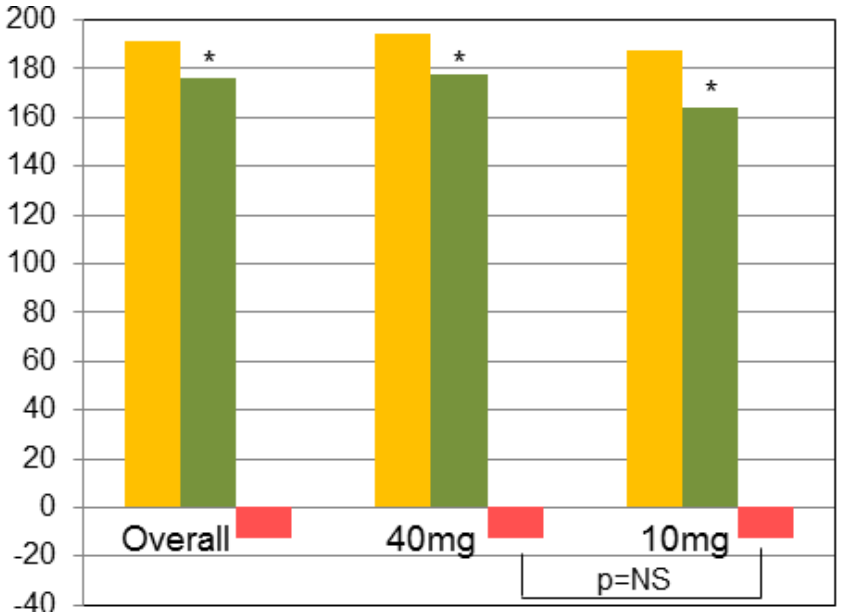


	Baseline	1 year
Lumen, mm^2	4.4	3.7
EEM, mm^2	19.0	14.0
Plaque, mm^2	14.6	10.3
VH-%NC	30%	15%
VH-TCFA	+	–
OCT-TCFA	+	–

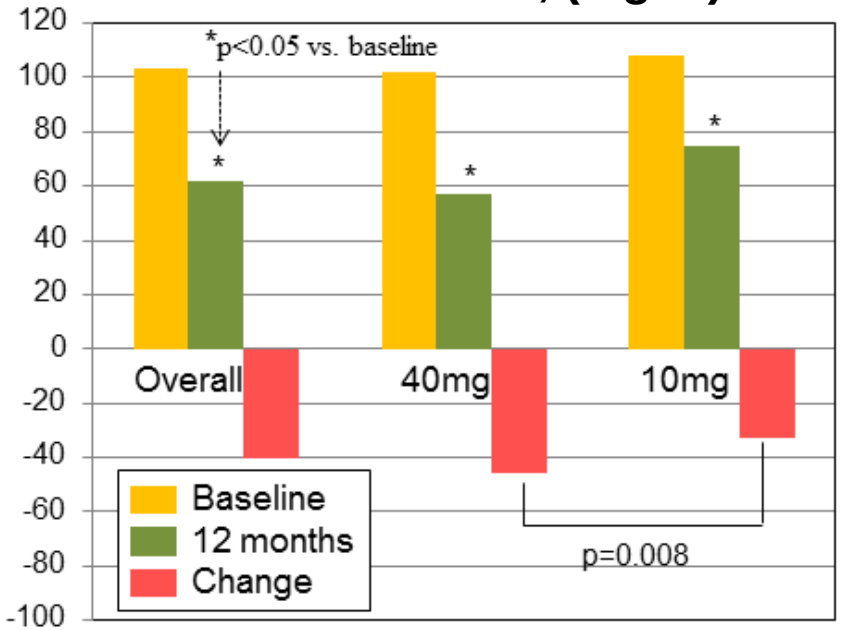
Primary Endpoint %NC volume (%)



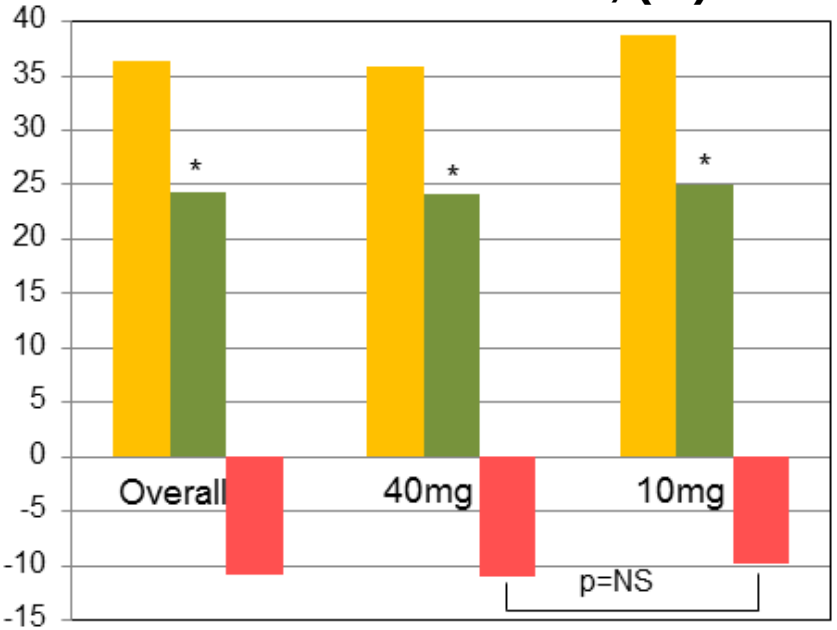
Normalized TAV, (mm³)



LDL cholesterol, (mg/dl)



%NC at index site, (%)



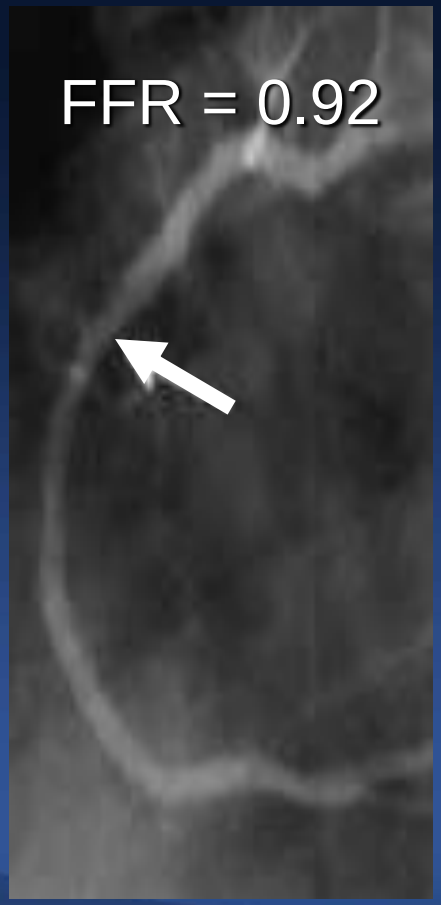
Clinical Outcomes at 12 months

- No cardiac death
- Culprit-related MACE: 4 (2.3%) pts. (3 TLR, 1 ST)
- NC-related MACEs: 8 (3.6%) pts. (7 TLR, 1 AMI)
- No difference in NC-MACE between rosuvastatin 40mg vs. 10mg (3.9% vs. 2.7%, p>0.05)

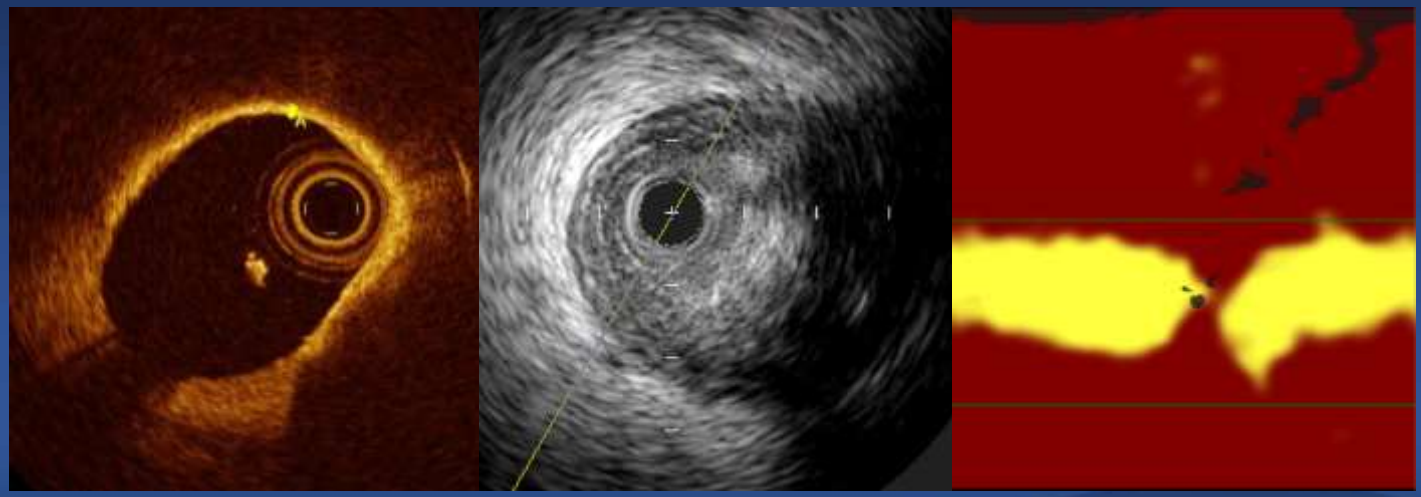
PREVENT Study,

The ***PREVENT***ive Implantation of BVS on Stenosis With Functionally Insignificant Vulnerable Plaque Compared to Optimal Medical treatment.

Functionally Insignificant (FFR >0.80), ***Vulnerable Plaque***



1. TCFA by OCT or VH-IVUS
2. PB_{MLA} ≥70%
3. MLA ≤4.0 mm^2
4. LRP on NIRS ($_{max}LCBI_{4mm}$>500)



PREVENT Trial

Any Epicardial Coronary Stenosis **with**
FFR ≥0.80 **and with** ***Two*** **of the following**

1. TCFA by OCT or VH-IVUS
2. IVUS MLA ≤4.0mm^2
3. IVUS Plaque Burden >70%
4. Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>500)

R

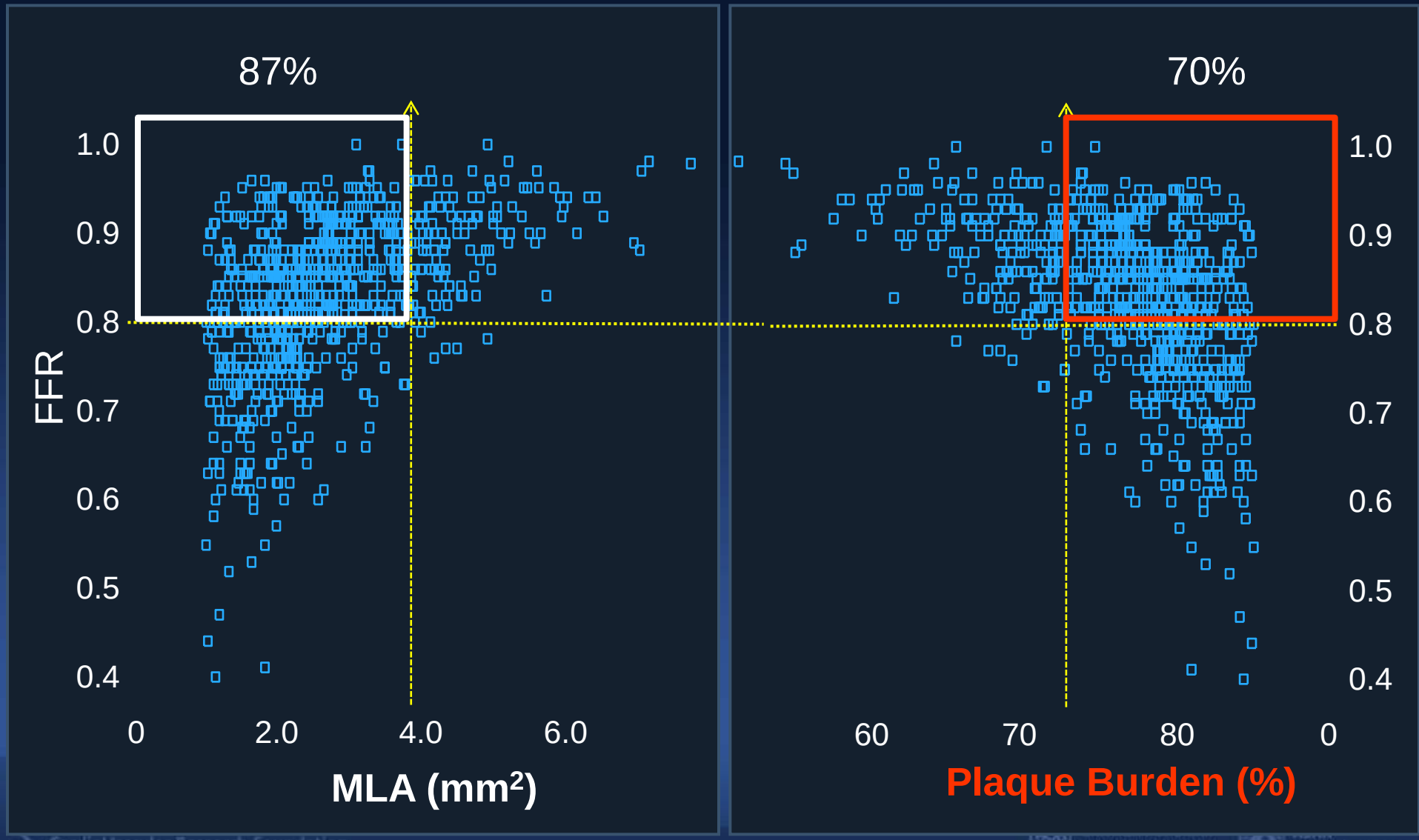
BVS+OMT
N=1000

OMT
N=1000

Primary endpoint *at 2 years*:
CV death, MI, Hospitalization d/t unstable angina

OCT sub-study/ NIRS sub-study, (300 patients in each arm at 2 years)

Patients Candidate



Objective,

To determine whether BVS implantation on functionally insignificant vulnerable plaque, reduce the incidence of the composite of MACEs compared with optimal medical therapy alone.

A prospective, randomized, multicenter, clinical trial with ‘all comers’ design. Approximately 2,000 patients will be enrolled from international heart centers.

Inclusion Criteria

Age 18 years or older,
Symptomatic or asymptomatic coronary stenosis,
Eligible for PCI, with
FFR >0.80 and met the two of the following

1. TCFA by OCT or VH-IVUS
2. IVUS MLA<4mm2
3. IVUS plaque burden>70%
4. Lipid-rich plaque on NIRS ($_{max}LCBI_{4mm}$>500)

Exclusion Criteria

Contraindication to dual antiplatelet therapy, Life expectancy <2y, Planned cardiac surgery or planned major non cardiac surgery, Preferred treatment for CABG, STEMI, Bypass graft lesion, Woman who are breastfeeding, pregnant or planning to become pregnant during the course of the study.

Primary and Major Secondary End Point,

The primary endpoint is the 2-year MACE (cardiovascular death, nonfatal MI, unplanned rehospitalization due to unstable angina).

The secondary endpoints include overall MACE, non-urgent revascularization, and rate of cerebrovascular event.

PREVENT Trial

Principal Investigators
Seung-Jung Park, MD, PhD. Korea

Co-Principal Investigator
Gregg Stone, MD, PhD. USA

Active Participants
Major 10 centers more in Korea
Takashi Akasaka, MD. Japan
3-4 centers more in Japan
Paul Kao, MD. Taiwan China
Huay Cheem Tan,MD.Singapore
Michael Lee, HongKong
David Smyth, MD. New Zealand
Ron Waksman, MD. USA
Alan Young, MD.USA
David Cohen, MD. USA
Antonio Colombo, MD. Italy